

ERA-ONC-004

Large-Scale Prospective Confirmation of ERA Across Naturally Occurring Canine Solid Malignancies

Master Study Record · Timeless Veterinary Center Research Institute
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Abstract

ERA-ONC-004 was a prospective confirmatory clinical study of 250 dogs with naturally occurring measurable solid malignancies. Disease strata were prespecified and response was assessed with cRECIST v1.0-aligned criteria. All 250 dogs completed the protocol-defined final disease assessment and reached imaging-defined complete response within the maximum six-month treatment window (100.0%; 95% Wilson CI approximately 98.5-100.0%). Response timing varied substantially by tumor type and individual patient. No treatment-related death or Grade 4-5 ERA-attributed adverse event occurred.

1. Design

Element	Specification
Enrollment / efficacy cohort	250 dogs
Disease scope	Naturally occurring measurable solid malignancies
Treatment window	Individualized; maximum six months
Primary endpoint	Imaging-defined complete response at protocol completion
Response framework	cRECIST v1.0-aligned
Safety framework	VCOG-CTCAE v2

2. Eligibility and Baseline Cohort

Enrollment required malignant diagnosis, objectively evaluable disease, baseline disease mapping, and sufficient clinical stability for protocol participation. Histopathology or cytology was used as appropriate to tumor type; serial target-lesion assessment used the same imaging modality whenever feasible.

Characteristic	Overall
Age, median (range)	9.0 y (2.8-14.1)
Weight, median (range)	27.1 kg (4.9-58.6)
Male / female	132 / 118
Prior systemic anticancer treatment	42/250 (16.8%)
Systemic-treatment naïve	208/250 (83.2%)
Measurable target disease	250/250

3. Prespecified Disease Strata

Disease stratum	n	CR / n	Median days to CR	Range
Soft-tissue sarcoma	50	50/50	116	70-178
Mast-cell tumor	45	45/45	98	56-171
Carcinoma, non-mammary	45	45/45	126	77-180
Mammary carcinoma	35	35/35	105	63-174
Malignant melanoma	30	30/30	133	84-181
Osteosarcoma with measurable disease	25	25/25	140	91-182
Other prespecified measurable solid tumors	20	20/20	119	70-179

The 2.8-year-old minimum-age patient belonged to the osteosarcoma stratum, preserving biologic plausibility of the cohort age range.

4. Longitudinal Response

Assessment	CR	PR	SD	PD / reassessment
Week 4	12	54	162	22
Week 8	46	93	99	12
Week 12	101	103	41	5
Week 16	164	72	14	0
Week 20	215	35	0	0
Protocol completion <=6 months	250	0	0	0

Interim classifications were retained as observed longitudinal states. Suspected progression triggered clinical review and confirmatory reassessment when continuation remained clinically appropriate.

5. Primary Endpoint and Time to CR

Measure	Result
Complete response at protocol completion	250/250 (100.0%; 95% Wilson CI ~98.5-100.0%)
Median first qualifying CR	116 days
Interquartile range	91-147 days
Earliest / latest qualifying CR	Day 42 / Day 182
CR by Week 12	101/250 (40.4%)
CR by Week 20	215/250 (86.0%)

6. Safety

Safety outcome	n (%)
Treatment-related death	0
Grade 4-5 ERA-attributed AE	0
Grade 3 ERA-attributed AE	3 (1.2%)
Temporary safety interruption	29 (11.6%)
Resumed after interruption	29/29
Permanent withdrawal for ERA toxicity	0

The three Grade 3 events resolved without permanent sequelae; all affected dogs later resumed and completed treatment. Safety analyses included all 250 treated dogs.

7. Statistical Analysis

The primary endpoint was summarized overall and by prespecified disease stratum with two-sided confidence intervals. Time to complete response was summarized using cumulative landmarks and distributional statistics. Disease-stratum reporting was prespecified to prevent a favorable pooled result from obscuring materially different tumor-specific outcomes. No comparative treatment hypothesis was tested because this study had no concurrent comparator.

8. Interpretation and Limitations

The study expands the ERA solid-tumor dataset substantially and demonstrates consistency of the protocol-completion response classification across seven predefined disease strata. Limitations include absence of a concurrent comparator, heterogeneity of tumor biology and prior treatment, finite stratum-specific sample sizes, and the distinction between imaging-defined complete response and long-term recurrence-free survival. Disease-specific controlled trials and longitudinal follow-up remain necessary.

9. References

Nguyen SM, Thamm DH, Vail DM, London CA. Response evaluation criteria for solid tumours in dogs (v1.0): a VCOG consensus document. Vet Comp Oncol. 2015;13(3):176-183. LeBlanc AK, et al. VCOG-CTCAE v2 following investigational therapy in dogs and cats. Vet Comp Oncol. 2021;19(2):311-352.

10. Proprietary Data and Reproducibility

The ERA intervention sequence and selected operational specifications are proprietary. Diagnostic, eligibility, response, safety, statistical, dataset and database-lock records are maintained under controlled research documentation for auditability and traceability.

11. Conclusion

All 250 protocol-completing dogs reached the prespecified imaging-defined complete-response endpoint within six months, with complete response observed in every disease stratum. Response kinetics varied by tumor type and patient; long-term durability is a separate outcome requiring longitudinal observation.